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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,521	03/17/2004	Daniel P. Wermeling	05062071	5461

26565 7590 11/02/2006

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EXAMINER	
YU, GINA C	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,521	WERMELING, DANIEL P.	
	Examiner	Art Unit	
	Gina C. Yu	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-26 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 05/18/2005, 07/12/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "an effective amount of a benzodiazepine or pharmaceutically acceptable salt thereof". Claim is vague and indefinite because there is no indication in the claim for what the drug is effective. Similarly, claim 11 recites "an effective amount of midazolam or pharmaceutically acceptable salt thereof", wherein the effective amount of the active ingredient is not defined.

The remaining claims are rejected as depending on the indefinite base claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Schweizer (US 5,166,202).

Schweizer discloses a method of treating panic disorder, panic attacks and the prevention of panic attacks to reduce anxiety by nasally administering midazolam and its pharmaceutically acceptable salts.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Fisgin et al. (J. Child Neurol. Dec. 2000).

Fisgin discloses a method of rapidly treating acute seizures of children in 5 minutes by nasally administering midazolam (5 mg/mL). See abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-10, 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schweizer in view of Haslwanter et al. (US 6565832 B1).

Schweizer teaches a method of treating panic disorder, panic attacks and the prevention of panic attacks to reduce anxiety by nasally administering midazolam and its pharmaceutically acceptable salts. The reference teaches administering 1-4 drops of an aqueous solution of midazolam, which is equivalent to 0.05-0.2 ml of the active ingredient. See col. 4, lines 41 – 53; instant claim 4. The reference teaches a nasal suspension in col. 3, lines 63- 66, meeting instant claim 7. Inducing general anesthesia by administering midazolam with other anesthetic agent is also taught. See col. 3, lines 8 – 10; instant claim 8.

Although Schweizer does not specifically indicate the formulation of the nasal composition, the reference teaches using pharmaceutically acceptable nasal carriers

that are well known in the art. See col. 3, lines 56 – 68. Particularly mentioned are glycols and glycol ethers for carriers.

Haslwanter teaches an aqueous nasal spray formulation which exhibits increased retention in the nasal cavity. The composition comprises up to 15 % by weight/volume of polyethylene glycol and a buffering agent to adjust the pH of the composition to 4-8. See col. 3, line 50 – col. 4, line 56; instant claims 6. The reference also teaches using glycerine, which is recited as a sweetener by applicants. See col. 4, lines 24 –34. See instant claims 1 and 9.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teaching of Schweizer by formulating a midazolam nasal composition, as motivated by Haslwanter, because 1) Schweizer specifically teaches to formulate a nasal composition of midazolam as well known in pharmaceutical art; and 2) Haslwanter teaches a general aqueous nasal spray formulation for medicaments, which exhibits increased retention in the nasal cavity. The skilled artisan would have had a reasonable expectation of successfully producing a stable nasal formulation comprising midazolam with increased drug retention in the nasal cavity, because both Schweizer and Haslwanter teach using glycols as the solvent.

Claims 5, 11, 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schweizer and Haslwanter as applied to claim 1-4, 6-10, 20-26 as above, and further in view of Craig et al. (US 5554639).

Haslwanter teaches in Example 6 a nasal spray composition comprising polyethylene glycol, propylene glycol, glycerine and an active ingredient.

The combined references fail to teach a preservative-free composition.

Craig teaches that a sterile, preservative-free nasal solution is preferred. See col. 3, lines 1 –4. Example formulations show an aqueous sterile composition comprising sodium saccharin and an active ingredient. See Examples 14-17; instant claims 5 and 11.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the nasal composition of the combined references to make a preservative-free nasal spray composition as motivated by Craig because it would be more desirable to use sterile formulation without preservatives. The skilled artisan would have had a reasonable expectation of successfully producing a preservative-free, sterile nasal formulation containing midazolam.

With respect to claims 16-19, the limitations are directed to the metabolism rate of the midazolam-containing composition. It is viewed that the obvious variation of the prior arts, which would comprise midazolam in a nasal carrier comprising polyethylene glycol and propylene glycol, and saccharide, would naturally have the metabolism rate as defined in the present claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 8, 10, and 11 of U.S. Patent No. 6,610271 B2 (" '271").

The '271 patent claims a sedative-anxiolytic nasal composition comprising lorazepam; 15-25 % by volume of polyethylene glycol and 75-85 % by volume of propylene glycol; and a sweetener. See '271, claims 1, 3, 6, 8, 10, and 11; instant claims 1, 2 and 9.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a composition comprising nasal carrier; lorazepam (a benzodiazepine); at least one or more sweeteners, flavoring agent, or masking agent; and the glycol solvent mixture in the same ratio.

Claims 3-8 and 10-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 8, 10, and 11 of '271 as applied to claims 1, 2, and 9 as above, and further in view of claims 9, 19, 21, 23, 24, 27 of '271 and Schweizer (US 5,166,202).

The '271 patent claims a formulation comprising polyethylene glycol, propylene glycol, and saccharide as recited in instant claim 11. See '271, claims 1, 9, 19, 21, 23, 24 and 27; instant claims 4, 7, 9, 11-14,

While the patent claims a nasal formulation for lorazepam and a method of treating anxiety-related disorders by using the composition, the patent does not teach midazolam.

Schweizer, as discussed above, teaches a method of treating panic disorder, panic attacks and the prevention of panic attacks to reduce anxiety by nasally administering midazolam and its pharmaceutically acceptable salts. See instant claim 3. The reference teaches administering 1-4 drops of an aqueous solution of midazolam, which is equivalent to 0.05-0.2 ml of the active ingredient. See col. 4, lines 41 – 53; instant claims 4 and 7. The reference teaches a nasal suspension in col. 3, lines 63-66, meeting instant claim 7. Inducing general anesthesia by administering midazolam with other anesthetic agent is also taught. See col. 3, lines 8 – 10; instant claims 8 and 15. The reference teaches that a relatively low dosage of midazolam is required for the treatment, and that the drug is well tolerated and easily administered. See col. 5, line 46 – col. 7, line 24.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the '271 invention by substituting lorazepam with midazolam because 1) both are art-recognized equivalents since they are well known anxiolytic drugs which are intranasally administered; and 2) Schweizer teaches that midazolam nasal spray is effective even in low dosage, well tolerated and easily administered.

The skilled artisan would have had a reasonable expectation of successfully producing a similar nasal composition for reducing anxiety. It is also viewed that the obvious variation of the prior arts, which would comprise midazolam in a nasal carrier comprising polyethylene glycol and propylene glycol, and saccharide, would naturally have the metabolism rate as defined in the present claims 16-19.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gina C. Yu whose telephone number is 571-272-8605. The examiner can normally be reached on Monday through Friday, from 8:00AM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gina C. Yu
Patent Examiner
9/30/06